REMARKS

For the convenience of the Examiner, this Reply is organized under appropriate subheadings.

Amendments to Claims 16, 17 and 52; and New Claims 75-104

Claims 16, 17 and 52 have been amended; and new Claims 75-104 have been added to more clearly define that which Applicants regard as the invention. Support for amendments to Claims 16, 17 and 52; and new Claims 75-104 can be found throughout the specification and the claims as originally filed.

For example, page 15, lines 28-30 and page 25, lines 12-18, describe treatment of chronic lymphocytic leukemia (CLL) and prostate cancer by administering cells that have been transfected with a miR15 gene product, thereby providing support for amendments to Claims 16, 17 and 52.

Page 25, lines 12-20 and page 26, lines 9-10 describe transfection of hematopoietic stem cells with a nucleic acid encoding a miR15 gene product, thereby providing support for new Claim 75.

Page 25, lines 18-22 and original Claim 26 describe transfection of cells with a plasmid or viral vector, thereby providing support for new Claims 76, 77, 91 and 92.

Page 17, lines 5-6 describe suitable promoters for expressing RNA from a plasmid, thereby providing support for new Claims 78 and 93.

Page 18, lines 27-30 describe suitable viral vectors for use in the claimed methods, thereby providing support for new Claims 79, 80, 94 and 95.

Page 27, lines 8-11 describe a plasmid expression vector that stably integrates into the genome of a cell to provide long-term expression, thereby providing support for new Claims 81, 82, 96 and 97.

Page 26, line 31 through page 27, line 2 describe introduction of a transfected cell into a subject by parenteral methods, thereby providing support for new Claims 83, 85 and 98.

Page 27, line 21 through page 28, line 3 describe suitable parenteral routes of administering a transfected cell to a subject, thereby providing support for new Claims 84 and 99.

Page 27, lines 4-6 describe suitable numbers of transfected cells for introduction into a subject, thereby providing support for new Claims 86 and 102.

Page 26, lines 5-8 describe isolation of CLL or prostate cancer cells from a subject, transfection of those cells with a nucleic acid encoding a miR15 gene product and reintroduction of the transfected cells into the subject, thereby providing support for new Claims 87 and 103.

Page 27, lines 6-7 describe culturing transfected cells prior to introduction into a subject, thereby providing support for new Claims 88 and 104.

Page 20, lines 5-7 describe inhibiting the neoplastic or tumorigenic growth of CLL or prostate cancer cells with miR15 or miR16 gene products, thereby providing support for new Claim 89.

Page 23, lines 9-11 describe a prostate cancer cell as including a cell located in the prostate, as well as a cell from a metastatic tumor of prostate origin, thereby providing support for new Claims 90 and 101.

Page 28, lines 3-5 describe administration of miR15 or miR16 gene products by injection into tumors, thereby providing support for new Claim 100.

Amendments to Claims 16, 17 and 52, and new Claims 75-104, do not add new matter. Entry is requested.

Sequence Non-Compliance

The specification was objected to because the description of FIG. 1A and FIG. 1B did not include references to SEQ ID NOS.

The specification has been amended, thereby obviating the objection.

Claim Objections

Claims 16, 17 and 52 were objected to because they depend from non-elected claims.

Applicants have amended Claims 16, 17 and 52, thereby obviating the objection.

Rejection of Claims 16, 17, 40-46, 48 and 52 under 35 U.S.C. § 112, First Paragraph

Claims 16, 17, 40-46, 48 and 52 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. In support of the rejection, the Examiner cited *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). The Examiner stated that the claims are directed to a method of treating or inhibiting proliferation of any miR15 mediated cancer or any miR15 mediated cancer cells in any subject. The Examiner also stated that the specification fails to provide sufficient guidance, including any relevant working examples, that would enable one of skill in the art to make and use the claimed invention. The Examiner further stated that it would require undue experimentation for one of skill in the art to make and use the claimed invention in light of the unpredictability of gene therapy, the breadth of the claims, and the lack of sufficient guidance in the specification.

Applicants have canceled Claims 40-46 and 48, thereby obviating the rejection for these claims.

In an embodiment, Applicants' claimed invention, as set forth in independent Claim 16, as amended, is directed to a method of treating chronic lymphocytic leukemia in a subject, comprising the step of administering a cell that has been transfected with a nucleic acid comprising a nucleotide sequence encoding a miR15 gene product to the subject.

In another embodiment, Applicants' claimed invention, as set forth in independent Claim 52, as amended, is directed to a method of treating a prostate cancer in a subject, comprising the step of administering a cell that has been transfected with a nucleic acid that comprises a nucleotide sequence encoding a miR15 gene product to the subject.

Dependent Claims 17, as amended, and 75-104 further limit independent Claims 16 and 52 by, *inter alia*, the cell, vector and route of administration employed in the methods of Claims 16 and 52.

Applicants have provided substantial guidance in the specification to enable one skilled in the art to transfect a cell with a nucleic acid comprising a nucleotide sequence encoding a miR15 gene product for use in treating chronic lymphocytic leukemia and prostate cancer in a subject, as set forth in pending Claims 16, 17 and 52, as amended, and new Claims 75-104. For example, page 13, lines 13-29 and Figure 1a describe miR15 gene products and sequences of

miR15 gene products, such as SEQ ID NOS:1 and 3. Page 25, line 23 through page 26, line 4; and page 43, line 1 through page 46, line 2 describe transfection of cells with nucleic acids encoding miR15 gene products and well established techniques to transfect cells.

Page 48, lines 6-25 describe methods to inhibit prostate tumor growth with, *inter alia*, a miR15 gene product.

Page 26, lines 5-10 describe cells for use in Applicants' claimed methods, including chronic lymphocytic leukemia cells, hematopoietic stem cells and prostate cancer cells. Page 22, line 7 through page 23, line 11; and page 43, line 1 through page 46, line 2 describe features, characteristics and methods of identifying chronic lymphocytic leukemia and prostate cancer cells for use in Applicants' claimed methods. Page 27, lines 6-11 describe culturing cells that have been isolated from a subject prior to transfection with a nucleic acid, and cells in which a nucleic acid vector has stably integrated into the genome.

Page 17, line 3 through page 20, line 4; and page 43, lines 1-29 describe suitable promoters, such as a U6 promoter, an H1 promoter, and a cytomegalovirus promoter, and vectors, including recombinant plasmid vectors, such as recombinant expression vectors, and recombinant viral vectors, such as adenoviral vectors, adeno-associated viral vectors, herpes viral vectors retroviral vectors, including lentiviral vectors, Rhabdoviral vectors, and murine leukemia virus vectors, for use in Applicants' claimed methods.

Page 26, line 31 through page 27, line 7 describe routes of administering the cells employed in Applicants' claimed methods, including parenteral administration, such as intravenous administration, intraarterial administration, peri-tissue injection, intra-tissue injection, subcutaneous injection, subcutaneous infusion, inhalation, and injection into bone marrow, as well as suitable numbers of cells for administration to a subject. Page 28, lines 3-5 describe administration by injection into a tumor.

Thus, one skilled in the art would be able to make a cell transfected with a nucleic acid encoding a miR15 gene product and administer the transfected cell to a subject, employing known techniques and the guidance of Applicants' specification. Therefore, Claims 16, 17 and 52, as amended, and new Claims 75-104 are enabled by the specification under 35 U.S.C. § 112, first paragraph.

SUMMARY AND CONCLUSION

The specification enables one of skill in the art to make and use the invention, as set forth in Claims 16, 17 and 52, as amended, and new Claims 75-104 and, thus, meets the requirement of 35 U.S.C. § 112, first paragraph. Therefore, Applicants respectfully request reconsideration and allowance of the claims under reconsideration. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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